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A heteroaromatic acid from marine sponge *Suberites vestigium*†

Prabhu Dutt Mishra*, Solimabi Wahidullah &
S Y Kamat
National Institute of Oceanography
Dona Paula, Goa 403 004, India

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4-Methyl- pyrazole-3(5)-carboxylic acid has been isolated from the butanol fraction of marine sponge, *Suberites vestigium* for the first time. The methanol extract of the sponge exhibits *in vitro* antihistaminic activity. Pyrazole derivatives as synthetic products are widely used as medicine, however, organic compounds containing pyrazole nucleus have not been reported from marine flora and fauna. Structure elucidation of the compound is based on spectral evidences.

In continuation of our work on bioactive metabolites from marine organisms, crude methanolic extract of marine sponge *Suberites vestigium* belonging to the order Hadromerida and family Suberitidae exhibited *in vitro* anti histaminic property. The search of active principle led us to isolate 4-methyl-pyrazole-3(5)-carboxylic acid from butanol fraction. To the knowledge of authors this is the first record of its natural occurrence, though pyrrole carboxaldehyde analogues have been reported from marine sponges[1] and soft corals[2,3]. The acid was obtained as colourless crystals. The UV and IR spectra was characteristic of an amino acid nucleus, [λ_{max} (MeOH), 265 (ε 3200), and ν_{max} (KBr) 3218-2818 cm^{-1}]. From NMR and mass spectra the elemental composition was determined as $C_5H_6N_2O_2$. All five carbons of the compound could be accounted for in the ^{13}CNMR spectrum and the chemical shifts were entirely compatible with a pyrazole type skeleton. This was further confirmed by the DEPT experiments revealing the presence of three quarternary, a methine and a methyl carbons. ^{1}HNMR of compound showed a methyl group on a sp^2 carbon at δ 1.92 and a vinyl proton at δ 7.3 as singlets. The two labile protons due to COOH and NH groups were evident at δ 12.2 and 13.0 (Deuterium exchangeable) respectively. Upfield resonance of methyl carbon indicated that methyl group is in proximity with COOH group. Long range coupling of vinyl proton with methyl protons ruled out the possibility of imidazole carboxylic acid and confirms the rigid structure of the molecule in COSY spectrum (Figure-1) as 4-methyl-pyrazole-3(5)- carboxylic acid 4.

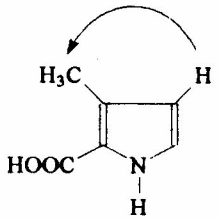

Figure 1 — 4-Methylpyrazole-3 (5)-carboxylic acid.

Experimental Section

The 10-15 Kg of sponge was collected from Mandapam, west coast of India, and extracted with methanol; the decants were filtered and concentrated by distillation under reduced pressure. The crude extract was suspended in aq. methanol (20%) and partitioned with pet. ether, chloroform, butanol. Butanol fraction was chromatographed over XAD-2 resin and eluted with water-methanol mixture in different proportions followed by repeated column chromatography over silica gel and elution with chloroform- methanol (8:2) to yield a colourless crystalline compound. NMR spectra were recorded on Bruker WM 400 MHz, FTNMR spectrometer, IR on Shimadzu FTIR- 8001 (KBr Pellet) and mass spectra on Jeol D-300 mass spectrometer at 70 ev.

4-Methyl-pyrazole-3(5)-carboxylic acid, Crystalline compound, m.p., 310-12 °C; UV (methanol): λ_{max} 265 (ε 3200); IR (KBr): 3218, 3062, 2818, 1760, 1674, 1648, 1556, 1474, 1380,

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1208, 842, 810 and 764 cm^{-1}; ^{1}HNMR (Pyridine-d_5, 400 MHz): δ 1.92 (3H, s), 12.2 (1H, bs), 13.0 (1H, bs), 7.3 (1H, s); ^{13}CNMR and DEPT: δ 12.2 (CH_3, 108 (C), 137 (CH), 153 (C), 166 (COOH); EIMS (m/z): 126 [M^+], 125, 112, 76, 83, 78, 55.

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